REMARKS

I. Claim Amendments

By the foregoing amendment, claims 1 and 46 have been amended to recite that the remyelinating agent is an antibody or an immunologically active fragment thereof that binds to alpha-4 beta-1 integrin, and that the administration of the remyelinating agent is chronic. Support for these amendments can be found throughout the specification and in original claims 9, 14, 17, and 50.

Claims 3, 6, 8, 11-14, 18, 52, and 56 have been amended to correct the dependencies and other minor editorial issues. Claim 16 has been amended to recite an effective blood level of natalizumab of "about 10 ng/ml or more," as supported at page 247 of the specification. No new matter has been added.

In addition, claims 14 and 17 have been a canceled without prejudice or disclaimer to the subject matter recited therein. Applicant reserve the right to file at least one continuation and/or divisional application directed to any canceled subject matter.

Entry of the foregoing amendments of the above-identified application are respectfully requested.

II. Response to Claim Objections

Claim 13 was objected to under 37 C.F.R. § 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. Claims 12 and 14 were objected to because they depend from "claim ii". Claim 16 was objected to because it recites an effective blood level of natalizumab of about "1 gnome."

In response, claim 13 has been amended to depend from claim 6. Claims 12 and 14 have been amended to depend from claim 11. In addition, claim 16 has been amended to recite an effective blood level of natalizumab of "about 10 ng/ml or more."

Accordingly, Applicants respectfully request reconsideration and withdrawal of the objections to the claims.

III. Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 11-16 and 55 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite because "natalizumab" is an arbitrary protein name that fails to distinctly claim the antibody.

This rejection is traversed for at least the following reasons. The Office states that natalizumab is simply the name given to a protein by various workers in the field. However, the name is in fact the United States Adopted Name (USAN) for the compound and not merely a name given to the protein by various workers. A USAN is the official non-proprietary or generic name given to a pharmaceutical substance. In the Specification, it is pointed out that natalizumab is the antibody also known as ANTEGREN® (now called TYSABRI®) (*see*, Specification at page 9, lines 14-16). As such, the name natalizumab particularly identifies the recited compound to anyone of ordinary skill in the art.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

IV. Response to Claim Rejections Under 35 U.S.C. § 112, First Paragraph

A. Claims 11-16 and 55 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly requiring a deposit of the hybridoma that produces the antibody natalizumab to satisfy the enablement requirement.

Applicants traverse this rejection for at least the following reasons. U.S. Patent No. 5,840,299, which has been incorporated by reference into the present Specification (*see*, e.g., Specification at page 29, lines 22-24), describes how to make a recombinant humanized anti-alpha-4 integrin antibody, including natalizumab. DNA encoding the recombinant antibody could be made by reference to the teaching of U.S. Patent No. 5,840,299 using routine synthetic and molecular biology methods. No deposit is required, where the required biological materials can be obtained from publicly available material with only routine experimentation and a reliable screening test. M.P.E.P. § 2404.02 (citing Tabuchi v. Nubel, 559 F.2d 1183, 194 U.S.P.Q. 521 (C.C.P.A. 1977); Ex Parte Hata, 6 U.S.P.Q.2d 1652 (Bd. Pat. App.

& Int. 1987)). Consequently, a deposit of a cell line producing natalizumab is not necessary to enable the presently claimed invention.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

B. Claims 1-24 and 46-59 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to meet the enablement and written description requirements.

The Office acknowledged that the Specification enables and describes a method of promoting remyelination of nerve cells or reversing paralysis in an MS patient using an anti-VLA-4 antibody (anti-alpha-4 beta-1 integrin antibody). However, the Office indicated that the Specification does not enable and/or describe other antibodies with the claimed function, because a person of ordinary skill in the art would not know which other antibodies could be used to promote remyelination of nerve cells or reverse paralysis. In addition, the Office stated that the EAE animal model system for MS used in the Specification cannot be relied on to predict whether anti-VLA-4 antibodies would promote remyelination of nerves in other disease conditions.

In response to the Office's position with regard to "remyelinating agents," Applicants note that the claims have been amended to recite "antibodies or immunologically active fragments thereof that bind to alpha-4 beta-1 integren."

In response to the Office's position with regard to disease conditions, Applicants respectfully traverse this rejection, as it may apply to the amended claims, for at least the following reasons. As noted in detail at pages 35 to 45 of the present specification, all of the diseases recited in the present claims, including MS, involve demyelination. Accordingly, Applicants submit that a person of ordinary skill in the art would have reasonably predicted, based on the EAE animal studies, that anti-VLA-4 antibodies would promote remyelination of the nerves not only in MS but also in the other recited disease conditions.

Applicants respectfully request reconsideration and withdrawal of the § 112, first paragraph rejections.

V. Response to Claim Rejections Under 35 U.S.C. § 102

A. Claims 1-4 and 46-48 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Cannella et al. (PNAS 95:10100-10105, 1998). Specifically, the Office indicated that Cannella et al. teaches methods of promoting remyelination in nerve cells in an MS patient using glial growth factor 2.

As noted above, the claims have been amended to recite that the remyelinating agents are "antibodies or immunologically active fragments thereof that bind to alpha-4 beta-1 integren." Cannella et al. does not disclose the recited remyelinating agents.

B. Claims 1-8 and 46-48 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Warrington et al. (PNAS 97:6820-6825, 2000). Specifically, the Office stated that Warrington et al. teaches methods of promoting remyelination in nerve cells in an MS patient using a mAb reactive to oligodendrocytes.

Similar to Canella et al., Applicants submit that Warrington does not disclose remyelinating agents that are "antibodies or immunologically active fragments thereof that bind to alpha-4 beta-1 integren."

C. Claims 1-17, 19-20, 24, 46-55, 57 and 58 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by WO 0015247.

According to the Office, WO 0015247 teaches methods of promoting remyelination in nerve cells in a multiple myeloma patient using mouse anti-VLA-4 mAbs, including humanized mAbs. The Office stated that the same dose is described, and concluded that while '247 does not explicitly indicate that the mAbs can cause remyelination of nerve cells or reversal of paralysis, such properties would be inherent.

Applicants respectfully traverse this rejection, as it may apply to the amended claims, for at least the following reasons.

WO 0015247 discloses methods of using integrin antagonists for treating multiple myeloma. As noted by the Office on page 10 of the outstanding Office Action, WO 0015247 does not explicitly recite chronic administration. The present

claims have been amended to recite that the claimed agents are administered chronically and Applicants note they have further discovered the benefits of chronic administration of the claimed remyelination agents.

D. Claims 1-17, 46-48 and 50-55 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,840,299.

The Office stated that US 5,840,299 teaches methods of promoting remyelination in nerve cells in an MS patient using humanized mAb 21.6 (natalizumab). The Office concluded that remyelination of nerve cells and reversal of paralysis would be inherent in the reference methods.

As noted above, claims 1 and 46 have been amended to recite that the remyelinating agent is administered chronically. As noted by the Office on page 10 of the outstanding Office Action, U.S. Patent No. 5,840,299 does not explicitly recite chronic administration. In the present invention, Applicants have further discovered the benefits of chronic administration of the claimed remyelination agents.

According to the above, Applicants respectfully request reconsideration and withdrawal of the § 102 rejections.

VI. Response to Claim Rejections Under 35 U.S.C. § 103

A. Claims 1, 17-18, 46, 50, 51 and 56 were rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 00/15247 or U.S. Patent No. 5,840,299.

B. Claims 1-4, 19-21, 49, 57 and 58 were rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 00/15247 in view of U.S. Patent No. 6,284,473.

C. Claims 1-4, 19-20, 22-23, 49, 57 and 59 were rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 00/15247 or U.S. Patent No. 5,840,299, each in view of U.S. Patent No. 6,753,135.

D. Claims 1-4, 19-21, 57 and 58 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,840,299 in view of U.S. Patent No. 6,602,885.

In order to establish a case of *prima facie* obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference or combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art reference(s) must teach or suggest all of the claim limitations. *See* M.P.E.P. § 2142. Applicants respectfully submit that these criteria have not been met in the present Office Action.

For the reasons set forth above in the response to the § 102 rejections over WO 00/15247 and U.S. Patent No. 5,840,299 do not teach or suggest the present claims. In addition, the additional references cited by the Office do not remedy the deficiencies of WO 0015247 and U.S. Patent No. 5,840,299. As stated by the Office, U.S. Patent No. 6,284,473 discloses that recombinant interferon beta-1b can affect MS. U.S. Patent No. 6,753,135 discloses that prednisone and related compounds may be used to treat MS. U.S. Patent No. 6,602,885 discloses agents which may be combined with CCR5 antagonists to treat MS or inflammatory bowel disease. Thus, these references fail to remedy the primary references cited by the Office. Further, there is no motivation to combine the secondary references cited by the Office with WO 0015247 and U.S. Patent No. 5,840,299.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the § 103 rejections.

Respectfully submitted,

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